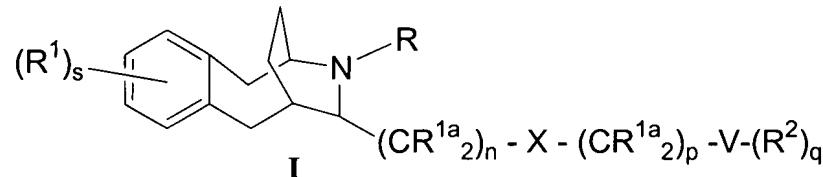


Please amend the claims as shown below:

1. (Currently Amended) A compound of Formula I



wherein

R is selected from

- 1) H,
- 2) ~~OR⁴;~~
- 3) unsubstituted or substituted C₁-C₁₀ alkyl,
- 4) unsubstituted or substituted aryl,
- 5) ~~unsubstituted or substituted C₃-C₁₀ cycloalkyl,~~
- 6) unsubstituted or substituted heterocycle,
- 7) ~~C(O)R⁴,~~
- 8) ~~C(O)OR⁴, and~~
- 9) ~~C(O)N(R⁴)₂;~~

R^{1a} is independently selected from

- 1) H,
- 2) unsubstituted or substituted C₁-C₆ alkyl, and
- 3) ~~OR⁴;~~

R^{1b} is independently selected from

- 1) H, and
- 2) unsubstituted or substituted C₁-C₆ alkyl;

X is selected from

- 1) a bond,
- 2) C(O), and
- 3) O, and

4) $\text{NR}^4;$

R^1 is independently selected from

- 1) H,
- 2) halo,
- 3) $\text{OR}^4,$
- 4) $\text{NO}_2,$
- 5) $\text{S(O)}_m\text{R}^4;$
- 6) CN
- 7) unsubstituted or substituted C₁-C₁₀ alkyl,
- 8) ~~unsubstituted or substituted aryl,~~
- 9) ~~unsubstituted or substituted C₂-C₆ alkenyl,~~
- 10) ~~unsubstituted or substituted C₃-C₁₀ cycloalkyl,~~
- 11) ~~unsubstituted or substituted alkynyl,~~
- 12) ~~unsubstituted or substituted heterocycle,~~
- 13) $-\text{C(O)R}^4,$
- 14) $\text{C(O)OR}^4,$
- 15) $\text{C(O)N(R}^4)_2,$
- 16) $\text{S(O)}_m\text{N(R}^4)_2,$ and
- 17) $\text{N(R}^4)_2;$

V is selected from aryl and heterocycle:

- 1) H,
- 2) $\text{CF}_3,$
- 3) aryl,
- 4) heterocycle, and
- 5) C₃-C₁₀ cycloalkyl;

R^2 is independently selected from

- 1) H,
- 2) unsubstituted or substituted C₁-C₁₀ alkyl,
- 3) $-(\text{CR}^{1b})_t\text{OR}^4,$
- 4) Halo,

- 5) CN,
- 6) NO₂,
- 7) CF₃,
- 8) -(CR^{1b})_tN(R⁴)₂,
- 9) -C(O)OR⁴,
- 10) -C(O)R⁴,
- 11) ~~S(O)R⁴~~,
- 12) -(CR^{1b})_tNR⁴(CR^{1b})_tR⁵,
- 13) -(CR^{1b})_tS(O)_mNR⁴,
- 14) -C(O)OR⁴R⁵,
- 15) -NR⁴C(O)R⁴,
- 16) ~~unsubstituted or substituted aryl, and~~
- 17) ~~unsubstituted or substituted heterocycle;~~

R⁴ is independently selected from

- 1) H,
- 2) unsubstituted or substituted C₁-C₁₀ alkyl,
- 3) unsubstituted or substituted C₃-C₁₀ cycloalkyl,
- 4) unsubstituted or substituted aryl,
- 5) unsubstituted or substituted heterocycle, and
- 6) CF₃;

R⁵ is independently selected from

- 1) unsubstituted or substituted aryl, and
- 2) unsubstituted or substituted heterocycle;

m is independently 0, 1 or 2;

n is 0 to 6;

p is 0 to 6;

q is 0 to 6, provided that when V is H or CF₃, q is 0; and

s is 0 to 16;

t is independently 0 to 6;

or a pharmaceutically acceptable salt or stereoisomer thereof.

2. (Currently Amended) The compound according to Claim 1 wherein R^{1b}, R⁴, R⁵ and variables m, n, p, q and t are as defined in Claim 1 and

R is selected from

- 1) H,
- 2) ~~OR⁴,~~
- 3) unsubstituted or substituted C₁-C₁₀ alkyl, and
- 4) ~~unsubstituted or substituted aryl.~~

R^{1a} is independently selected from

- 1) H, and
- 2) unsubstituted or substituted C₁-C₆ alkyl;

X is selected from

- 1) a bond, and
- 2) C(O);

R¹ is independently selected from

- 1) H,
- 2) halo,
- 3) OR⁴,
- 4) N(R⁴)₂,
- 5) NO₂, and
- 6) ~~unsubstituted or substituted C₁-C₁₀ alkyl;~~

V is selected from aryl and heterocycle:

- 1) ~~H,~~
- 2) ~~CF₃,~~
- 3) ~~aryl, and~~
- 4) ~~heterocycle;~~

R² is independently selected from

- 1) H,
- 2) unsubstituted or substituted C₁-C₁₀ alkyl,
- 3) $(CR^{1b})_t OR^4$,
- 4) Halo,
- 5) CN,
- 6) NO₂,
- 7) CF₃,
- 8) $(CR^{1b})_t N(R^4)_2$,
- 9) C(O)OR⁴,
- 10) $(CR^{1b})_t S(O)_m NR^4$,
- 11) $(CR^{1b})_t NR^4 (CR^{1b})_t R^5$,
- 12) C(O)OR⁴R⁵, and
- 13) NR⁴C(O)R⁴;

s is 0 to 6;

or a pharmaceutically acceptable salt or stereoisomer thereof.

3. (Currently Amended) The compound according to Claim 1 wherein R^{1b}, X, R¹, R², R⁴, R⁵ and variables m and t are as defined above and:

R^{1a} is independently selected from

- 1) H, and
- 2) unsubstituted or substituted C₁-C₆ alkyl;

V is phenyl; selected from

- 1) aryl, and
- 2) heterocycle;

n is 0 or 1; to 3;

p is 0 to 3;

q is 0 to 3;

or a pharmaceutically acceptable salt or stereoisomer thereof.

4. (Original) A compound that is:

(6*R*,9*S*,11*R*)-11-phenyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [a][8]annulene;

(6*R*,9*R*,11*S*)-11-phenyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [a][8]annulene;

(6*S*,9*R*,11*R*)-11-phenyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [a][8]annulene;

(6*S*,9*R*,11*S*)-11-phenyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [a][8]annulene;

(6*S*,9*R*,11*S*)-11-benzyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [a][8]annulene;

(6*S*,9*R*,11*R*)-11-benzyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [a][8]annulene;

(6*R*,9*S*,11*S*)-11-benzyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [a][8]annulene;

(6*R*,9*S*,11*R*)-11-benzyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [a][8]annulene;

(6*S*,9*R*,11*S*)-11-(3-bromobenzyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)
benzo[a][8]annulene;

(6*S*,9*R*,11*R*)-11-(3-bromobenzyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)
benzo[a][8]annulene;

(6*R*,9*S*,11*S*)-11-(3-bromobenzyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)
benzo[a][8]annulene;

(6*R*,9*S*,11*R*)-11-(3-bromobenzyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)
benzo[a][8]annulene;

(6*S*,9*R*,11*S*)-11-(1,3-benzodioxol-5-ylmethyl)-5,6,7,8,9,10-hexahydro-6,9-
(epiminomethano)benzo[a][8]annulene;

(6*S*,9*R*,11*R*)-11-(1,3-benzodioxol-5-ylmethyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulene;

(6*R*,9*S*,11*S*)-11-(1,3-benzodioxol-5-ylmethyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulene;

(6*R*,9*S*,11*R*)-11-(1,3-benzodioxol-5-ylmethyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulene;

(6*S*,9*R*,11*S*)-11-(3-bromobenzyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulen-4-amine;

(6*S*,9*R*,11*R*)-11-(3-bromobenzyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulen-4-amine;

(6*R*,9*S*,11*S*)-11-(3-bromobenzyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulen-4-amine;

(6*R*,9*S*,11*R*)-11-(3-bromobenzyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulen-4-amine;

(6*S*,9*R*,11*S*)-11-(3-bromobenzyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulen-1-amine;

(6*S*,9*R*,11*R*)-11-(3-bromobenzyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulen-1-amine;

(6*R*,9*S*,11*S*)-11-(3-bromobenzyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulen-1-amine;

(6*R*,9*S*,11*R*)-11-(3-bromobenzyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulen-1-amine;

(6*S*,9*R*,11*S*)-11-(1-benzofuran-2-ylmethyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulene;

(6*S*,9*R*,11*R*)-11-(1-benzofuran-2-ylmethyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulene;

(6*R*,9*S*,11*S*)-11-(1-benzofuran-2-ylmethyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulene;

(6*R*,9*S*,11*R*)-11-(1-benzofuran-2-ylmethyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulene;

(6*S*,9*R*,11*S*)-11-(1,3-oxazol-2-ylmethyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulene;

(6*S*,9*R*,11*R*)-11-(1,3-oxazol-2-ylmethyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulene;

(6*R*,9*S*,11*S*)-11-(1,3-oxazol-2-ylmethyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulene;

(6*R*,9*S*,11*R*)-11-(1,3-oxazol-2-ylmethyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulene;

(6*S*,9*R*,11*S*)-11-isopentyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [*a*][8]annulene;

(6*S*,9*R*,11*R*)-11-isopentyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [*a*][8]annulene;

(6*R*,9*S*,11*S*)-11-isopentyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [*a*][8]annulene;

(6*R*,9*S*,11*R*)-11-isopentyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [*a*][8]annulene;

or a pharmaceutically acceptable salt or stereoisomer thereof.

5. (Original) A compound according to Claim 4 that is:

(6*R*,9*S*,11*R*)-11-phenyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [a][8]annulene;

(6*R*,9*R*,11*S*)-11-phenyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [a][8]annulene;

(6*S*,9*R*,11*R*)-11-phenyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [a][8]annulene;

(6*S*,9*R*,11*S*)-11-phenyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [a][8]annulene;

or a pharmaceutically acceptable salt or stereoisomer thereof.

6. (Withdrawn) A pharmaceutical composition which is comprised of a compound in accordance with Claim 1 and a pharmaceutically acceptable carrier.

7. (Withdrawn) A method of modulating the catalytic activity of protein kinases in a mammal in need thereof comprising contacting the protein kinase with a compound of Claim 1.

8. (Withdrawn) The method of Claim 7 wherein the protein kinase is an RTK.

9. (Withdrawn) The method of Claim 8, wherein the RTK is selected from IR, IGF-1R and IRR.

10. (Withdrawn) A method of treating or preventing a PK-related disorder in a mammal in need thereof comprising administering to said mammal a therapeutically effective amount of a compound of Claim 1.

11. (Withdrawn) A method of Claim 10, wherein the PK-related disorder is an IGF-1R-related disorder selected from:

- 1) cancer,
- 2) diabetes,
- 3) an autoimmune disorder,
- 4) a hyperproliferation disorder,

- 5) aging,
- 6) acromegaly, and
- 7) Crohn's disease.

12. (Withdrawn) A method of treating cancer in a mammal in need of such treatment comprising administering to said mammal a therapeutically effective amount of a compound of Claim 1.

13. (Withdrawn) A method of treating retinal vascularization comprising administering to a mammal in need of such treatment a therapeutically effective amount of a compound of Claim 1.

14. (Withdrawn) A method of treating cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with a second compound selected from:

- 1) an estrogen receptor modulator,
- 2) an androgen receptor modulator,
- 3) retinoid receptor modulator,
- 4) a cytotoxic agent,
- 5) an antiproliferative agent,
- 6) a prenyl-protein transferase inhibitor,
- 7) an HMG-CoA reductase inhibitor,
- 8) an HIV protease inhibitor,
- 9) a reverse transcriptase inhibitor, and
- 10) an angiogenesis inhibitor.

15. (Withdrawn) The method of Claim 14, wherein the second compound is an estrogen receptor modulator selected from tamoxifen and raloxifene.

16. (Withdrawn) A method of treating cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with radiation therapy.

17. (Withdrawn) The method of Claim 16 wherein radiation therapy is also administered.

18. (Withdrawn) A method of treating cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 and paclitaxel or trastuzumab.

19. (Withdrawn) A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 and a GPIIb/IIIa antagonist.

20. (Withdrawn) The method of Claim 19 wherein the GPIIb/IIIa antagonist is tirofiban.

21. (Withdrawn) A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with a COX-2 inhibitor.